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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| KERR, KATHLEEN M | |
| ART UNIT | PAPER NUMBER |
| 1652 | |

DATE MAILED: 04/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/767,680 | GEPPEL ET AL. | |
| | Examiner | Art Unit | |
| | Kathleen M Kerr | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 and 4-57* is/are pending in the application.

4a) Of the above claim(s) *18-33 and 53-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-17,34-52,56 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/2/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Application Status*

1. In response to the previous Office action, a non-final rejection (mailed on August 1, 2003), Applicants filed a response and amendment received on February 2, 2004 and (corrected) on September 7, 2004. Said amendment amended Claims 1, 4-12, 17, 34, and 36-52 and added new Claims 56-57. Thus, Claims 1 and 4-57 are pending in the instant Office action.

### *Restriction/Election*

2. Newly filed claims 56-57 are drawn to the elected invention. Claims 1 and 4-57 are pending in the instant application. Claims 1, 4-17, 34-52 and 56-57 are drawn to the elected invention and will be examined herein. Claims 18-33 and 53-55 are withdrawn from further consideration as non-elected inventions.

### *Priority*

3. As previously noted, the instant application is granted the benefit of priority as the continuation of PCT/DK01/00036 filed on January 18, 2001 and as a continuation-in-part of U.S. non-provisional Application No. 09/488,644 filed on January 21, 2000.

### *Information Disclosure Statement*

4. The information disclosure statement filed on February 2, 2004 has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

***Withdrawn - Objections to the Specification***

5. Previous objection to the specification for being confusing concerning porphyrin content throughout the examples presented is withdrawn by virtue of the Examiner's reconsideration. The Examples specifically describe the quantitation of either haemin or cytochrome d in the treated lactic acid bacterial cells and not the quantitation of generic porphyrin. Thus, while the Examples do not provide enabling support for the claimed invention (see rejections under 35 U.S.C. § 112, first paragraph, below), they are clear.

***Withdrawn - Objections to the Claims***

6. Previous objection to Claim 14 for having improper punctuation is withdrawn. While the claims would be clearer written as ---frozen composition, liquid composition, or freeze-dried composition---, this can be interpreted from the claims as pending presently and the Examiner cannot require such an amendment.

***Maintained - Claim Rejections - 35 U.S.C. § 112, second paragraph***

7. Previous rejection of Claims 8 and 9 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "about" is maintained. Applicants' arguments have been fully considered but are not deemed persuasive. Applicants argue that if the claims are read in light of the specification, the term "about" is clear. The Examiner disagrees. No indication of the +/- of the term "about" is indicated in the specification. By Applicant's own admission, the term "about" is "not definite" (see remarks filed February 2, 2004, page 16). The specification gives no understanding of the indefinite term, thus, one of skill in the art would be unclear as to the metes and bounds of the claim's limitation.

8. Previous rejection of Claim 34 under 35 U.S.C. § 112, second paragraph, is maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. The Examiner withdraws the issue of antecedent basis in view of Applicant's arguments. However, Applicant fails to address the issue previously raised that

> "It is unclear if DSM12015 must be subjected to the porphyrin-containing substrate treatment or if DSM12015 already has the characteristics claimed in Claim 1."

Since the deposited strain is specific, as opposed to the species of Claim 6, it is unclear if the strain has been treated yet or not and/or if further treatment is required.

***Withdrawn - Claim Rejections - 35 U.S.C. § 112, first paragraph***

9. Previous rejection of Claim 34 under 35 U.S.C. § 112, first paragraph, enabling deposit, is withdrawn by virtue of Applicant's filing a statement certifying that all restrictions on accessibility to said deposit be irrevocably removed by Applicant upon the granting of the patent.

10. Previous rejection of Claim 11 under 35 U.S.C. § 112, first paragraph, scope of enablement, is withdrawn by virtue of Applicant's amendment.

***Maintained - Claim Rejections - 35 U.S.C. § 112, first paragraph***

11. Previous rejection of Claims 1, 4-17, 34-52 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for lactic acid bacterial cells modified to contain at least 0.1 ppm haemin, does not reasonably provide enablement for lactic acid bacterial cells modified to contain at least 0.1 ppm of ***any*** **porphyrin** containing compound

is maintained. Moreover, new Claims 56 and 57 are added to the instant rejection. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicant argues that the two working examples, when combined with the state of the art, fully enable the scope of the claimed invention; the Examiner disagrees. The examples teach how to achieve lactic acid bacteria retaining 41 ppm haemin (Example 1, see page 25) and 13 ppm cytochrome d (Example 2, see page 28) and not how to achieve particular levels and *any porphyrin*. While the Examiner agrees that the use of porphyrin compounds is well known in the art to affect bacterial growth, the claims require **retention** of porphyrin compounds to a specific extent (at least 0.1 ppm) and this is not enabled in the prior art.

The art (Zerr *et al.* and Leung *et al.*) cited by Applicant in response to the instant rejection, some of which is not prior art and cannot be cited to enable claims which must be enabled at the time of filing, teaches how porphyrin-containing compounds effect cell growth; no teachings of how or why porphyrin compounds might be retained in the cell upon inclusion in the fermentation media are found.

Applicant argues that because two working examples describing the steps of fermenting lactic acid bacteria in the presence of 10 mg/ml haemin are disclosed, the claims requiring retention of porphyrin compounds to a specific extent in the cells are enabled. Clearly all porphyrins do not act the same in a lactic acid bacterial cell as evidenced by Applicant's own data (41 ppm haemin and 13 ppm cytochrome d). While the predictability of *how* to administer porphyrin compounds to lactic acid bacterial cells is high, *the ability to retain* said porphyrins in the cell to the prescribed extent, as required to make the claimed product, is very low based on

the little data provided in the instant specification. As previously noted, all the Wands factors were considered, not just whether or not working examples were present:

> "In the instant application, *L. lactis* CHCC373 cells are treated with 10 mg/L haemin and grown in anaerobic or aerobic conditions. The cell extract (supernatant) and pellet (debris) were assayed. The assay described shows 41 ppm haemin found in the cell debris, i.e. associated with the cellular material, and not in the cell extract when cells are grown under anaerobic or aerobic conditions. Thus, 10 mg/L haemin-treated *L. lactis* cells retain 41 ppm haemin attached to their cellular material when cells are fermented under aerobic or anaerobic conditions. While minimal guidance in the use of other porphyrin-containing compounds is offered, **no other working examples** to help define the scope of the claims are described. The **state of the prior** art is such that numerous porphyrin compounds are known, but all have different cellular association characteristics with different bacteria. Therefore, it is wholly **unpredictable how to achieve the containment of at least 0.1 ppm of *any* porphyrin-containing compound** other than those demonstrated, i.e., haemin, in the specification and/or the art." (emphasis added)

12. Previous rejection of Claim 5 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for lactic acid bacterial cells modified to contain at least 0.1 ppm **cytochrome d** when fermented under aerobic conditions, does not reasonably provide enablement for lactic acid bacterial cells modified when fermented under **anaerobic** conditions is maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant's arguments only reiterate those cited above and are not specific to the enablement issue of interest in the instant rejection. Thus, the response provided above by the Examiner is sufficient to rebut Applicant's arguments.

13. Previous rejection of Claims 8-9 under 35 U.S.C. § 112, first paragraph, enablement, as failing to comply with the enablement requirement is maintained. To make the cells claimed that

will be effective when **inoculated** in a **concentration** of $10^7$ **cells/ml** into low pasteurized skimmed milk having **8 ppm of dissolved oxygen** would require undue experimentation. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant's arguments only reiterate those cited above and are not specific to the enablement issue of interest in the instant rejection. Thus, the response provided above by the Examiner is sufficient to rebut Applicant's arguments.

14. Previous rejection of Claim 9 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for lactic acid bacterial cells modified to consume **at least 50% of dissolved oxygen** with treatment under aerobic conditions, does not reasonably provide enablement for lactic acid bacterial cells modified when fermented under **anaerobic** conditions is maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant's arguments only reiterate those cited above and are not specific to the enablement issue of interest in the instant rejection. Thus, the response provided above by the Examiner is sufficient to rebut Applicant's arguments.

15. Previous rejection of Claim 12 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for lactic acid bacterial cells modified to reduce **LDH** activity by **at least 10%** with treatment under aerobic conditions, does not reasonably provide enablement for lactic acid bacterial cells modified when fermented under **anaerobic** conditions is maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant's arguments only reiterate those

cited above and are not specific to the enablement issue of interest in the instant rejection. Thus, the response provided above by the Examiner is sufficient to rebut Applicant's arguments.

16. Previous rejection of Claim 16 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for lactic acid bacterial cells modified to contain at least 0.1 ppm cytochrome d using mixed lactic acid bacterial strains grown aerobically, does not reasonably provide enablement for lactic acid bacterial cells modified to contain at least 0.1 ppm of **any porphyrin** containing compound **using pure strains** is maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant's arguments only reiterate those cited above and are not specific to the enablement issue of interest in the instant rejection. Thus, the response provided above by the Examiner is sufficient to rebut Applicant's arguments.

17. Previous rejection of Claims 40-42 under 35 U.S.C. § 112, first paragraph, enablement, as failing to comply with the enablement requirement is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention at "at least **60 ppm**" (emphasis added) or higher of a **porphyrin-containing compound**. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant's arguments only reiterate those cited above and are not specific to the enablement issue of interest in the instant rejection. Thus, the response provided above by the Examiner is sufficient to rebut Applicant's arguments.

18. Previous rejection of Claims 45-47 under 35 U.S.C. § 112, first paragraph, enablement, as failing to comply with the enablement requirement is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention at "at least **40 ppm**" (emphasis added) or higher of a **cytochrome**. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant's arguments only reiterate those cited above and are not specific to the enablement issue of interest in the instant rejection. Thus, the response provided above by the Examiner is sufficient to rebut Applicant's arguments.

19. Previous rejection of Claims 48-52 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for cells that, after having been treated with 10 mg/L haemin and inoculated into milk can reduce the amount of dissolved oxygen by about 35% per hour, does not reasonably provide enablement for cells otherwise treated that reduce the amount of dissolved oxygen **at greater than 35% per hour** is maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant's arguments only reiterate those cited above and are not specific to the enablement issue of interest in the instant rejection. Thus, the response provided above by the Examiner is sufficient to rebut Applicant's arguments.

***Maintained - Claim Rejections - 35 U.S.C. § 103***

20. Previous rejection of Claims 1, 4-7, 10-17, 35-39, 43, 44, 48, and 49 under 35 U.S.C. § 103(a) as being unpatentable over Kaneko *et al.* (USPN 5,075,226 – see IDS Paper No. 6) is

maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicant argues that although Kaneko *et al.* teach treatment of *L. lactis* cells with as much as 325 mg/L hemin, the claimed product would not have been produced because Kaneko *et al.* does not expressly disclose all the features of the claimed invention. The Examiner disagrees. Applicant notes a "difference in experimental protocol"; however, no differences are specifically cited. Since no indication of anything other than treatment of cells with 10 mg/L haemin produces the instantly claimed cells (these are the only working examples that support the claimed invention in the instant specification), Kaneko *et al.* necessarily teach the claimed cells. The only "combination" of references is to practice the invention of Kaneko *et al.* to the full extent of its scope (see Claim 3 of Kaneko *et al.*) and one of skill in the art is clearly motivated to do so as expressly provided by Kaneko *et al.* in the patent.

***Conclusion***

21. Claims 1, 4-17, 34-52 and 56-57 are not allowed for the reasons identified in the numbered sections of this Office action.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kathleen M Kerr
Primary Examiner
Art Unit 1652

November 20, 2004